REMARKS

The Final Office Action of June 1, 2007, has been carefully studied. Upon entry of the amendments presented above, the claims in the present application will be claims 1, 5, 6, 14, 17-21, 24-29 and 32-35. Applicants maintain that these claims define novel and unobvious subject matter under Sections 102 and 103 and should therefore be allowed. Favorable reconsideration, entry of the amendments presented above, and allowance are respectfully urged.

First, some amendments have been made to better focus the claims. Thus, one major change is the insertion of claim 3 into claim 1, claim 16 into claim 14, and claim 23 into claim 21, whereby claims 1, 14 and 21 correspond in large part to claims 3, 16 and 23 rewritten in independent form.

Claim 1 is further amended above to clarify, consistent with claim 14 as previously amended, that thrombin and fibrinogen are not present in such a way as to be able to react prior to use of the claimed hemostatic material. In other words, claim 1 is clarified so as to exclude any embodiment of a hemostatic material comprising thrombin and fibrinogen, both of which are held on a bioabsorbable synthetic nonwoven fabric in a way as to permit them to react prior to use of the claimed material. This clarification is

fully consistent with the improved results shown in applicants' specification.

Claims 1-6 and 14-35 have been finally rejected for the first time as obvious under Section 103 from Greenawalt (previously applied under Section 102) in view of newly cited and applied Geller et al, citation U (Geller) and Ikada et al USP 4,882,162 (Ikada). This rejection is respectfully traversed.

The PTO acknowledges that Greenawalt does "not teach a process of forming the nonwoven fabric comprising thrombin and fibrinogen, wherein the fabric being treated with thrombin first and then treated with fibrinogen…", but that without any reason provided by the prior art, it nevertheless "would have been obvious" to do so. Applicants respectfully submit that in the absence of any reason for any such modification in Greenawalt, and none is demonstrated by the PTO, the rejection does not comply with the requirements of MPEP 2143.

Applicants respectfully note that the newly applied subsidiary references do not provide any reason for such a modification in Greenawalt. The prior art does not lead the person of ordinary skill in the art to make the aforementioned proposed change in Greenawalt, and the rejection is therefore also not in compliance in this regard with *Ex parte* Levengood, 28 USPQ2d 1300, and In re Zurko, 42 USPQ2d 1476.

As noted above, claim 1 has been amended so that it clearly features: that a hemostatic material either consists of (i) thrombin held on a bioabsorbable synthetic nonwoven fabric and (ii) fibrinogen; or consists of (i) a bioabsorbable synthetic nonwoven fabric, (ii) thrombin and (iii) fibrinogen, and that a reaction does not occur between thrombin and fibrinogen till use, namely so as to exclude such an embodiment as a hemostatic material comprising thrombin and fibrinogen, both of which are held on a bioabsorbable synthetic nonwoven fabric.

In this regard, it should be noted that "a bioabsorbable synthetic nonwoven fabric made of polyglycolic acid" as used as a supporting material is inclined to firmly stiffen when fibrinogen is held thereon to thereby let the nonwoven fabric become substantially non-flexible, and hence quite unsuitable for use as hemostatic material. For this reason, before use, at least fibrinogen is not sprayed or applied to the nonwoven fabric in accordance with the present invention. More specifically, in preferable embodiments, a fibrinogen solution is applied to the polyglycolic acid nonwoven fabric holding thrombin immediately prior to use thereof, or alternatively, both a fibrinogen solution and a thrombin solution are sprayed onto the polyglycolic acid nonwoven fabric immediately prior to use thereof.

As noted above, Greenawalt does not lead the person of ordinary skill in the art to the use of a polyglycolic acid nonwoven fabric as a supporting material, and consequently to the above-mentioned preferable embodiments in accordance with the present invention with regard to thrombin and fibrinogen.

Moreover, regarding the feature of the "nonwoven fabric" which is one of the distinguishing features of the present invention, the rejection states that, although the Greenawalt product is described as "paper-like material"[1], it is mainly made of carboxymethyl cellulose (CMC) pulp (cellulose fiber) and/or polyglycolic acid (PGA), which would provide sufficient elasticity and flexibility as evidenced by Geller and Ikada and thus the product of Greenawalt would have inherent elasticity and flexibility to be formed into any shape.

However, paper is not elastic. It should be noted that the technique taught by Greenawalt is simply a technology of paper-making as described "using existing paper-making technology (e.g. *Handbook for Pulp & Paper Technologists*, Smook, G. 2nd edition, Angus Wilde Publications Inc., 1994) and as described in the examples, the pulp solution is collected, pressed and dried" (cf. col. 8, lines 43-54; col. 9, lines 8-13). Contrary to this, a nonwoven fabric as used

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[1] Greenawalt also uses the expressions "paper-like structure" and "paper-like compositions."

in the present invention is a nonwoven fabric made of polyglycolic acid such as used in the working examples of the instant application, e.g. "Neoveil" manufactured by Gunze Limited (page 8, lines 4-6).

Such a nonwoven fabric made of polyglycolic acid may be manufactured by needle-punching piled woven or knitted fabric into nonwoven fabric as shown in Japanese Patent Publication No. 18579/1993 filed by Gunze Limited (a copy is attached hereto together with its English language abstract) (*"The polymer is decomposed and absorbed into living body, and thus high affinity to living body can be attained and no side effect or undesirable effect to living body arises. The polymer includes polyglycolic acid, copolymer of glycolic acid and lactic acid, etc. The chips of the polymer are melt-spun to give multifilament, random web obtained from the multifilament is made into nonwoven fabric or woven or knitted fabric. The fabrics are piled and needle-punched, followed by pressing under heating and finally the resultant is cut into desirable size, from which pledget is obtained."*). Thus, the nonwoven fabric according to the present invention is well distinguished from the material made by paper-making technology disclosed in Greenawalt.

The Examiner further relies on Geller and Ikada. However, Geller merely teach the conditions of spinning for

carboxymethyl cellulose (CMC) whereas Ikada relates to an artificial skin characteristically consisting of a polymer support film, such as silicone rubber, and a fibrous material composed of bioabsorbable substance such as polyglycolic acid fixed on the polymer support film wherein the strength of said fibrous material is reduced by degradative treatment.[2] Therefore, even if Geller and Ikada were obviously combined together with Greenawalt, applicants maintain that it still would not have been obvious to one of ordinary skill in the art to use the polyglycolic acid nonwoven fabric in a hemostatic material involving the use of thrombin and fibrinogen.

The rejection further alleges with regard to the use of "organic solvent" in Greenawalt that, as all the examples in Greenawalt utilize ethanol as an organic solvent, and it is well known that carbon tetrachloride is toxic and an ozone-depleting gas, it would have been obvious to one of ordinary skill in the art not to use toxic organic solvents such as carbon tetrachloride, and to use ethanol instead.

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[2] Applicants have never alleged to be the inventor of polyglycolic acid fabric per se.

However, the present invention is quite distinct from the technique of Greenawalt in that no organic solvent such as ethanol is used in the present invention. It should be noted that the reason why Greenawalt utilizes an organic solvent is to avoid a reaction between thrombin and fibrinogen while making the paper-like product, both of which are present in one and the same system to form fibrin, as Greenawalt teaches that "*Since all of the precipitation, mixing and paper-making steps are in a non-aqueous solvent and not in water, the thrombin does not activate fibrinogen during processing.*" (cf. col. 8, lines 57-60).

To the contrary, in case of a hemostatic material according to the present invention, fibrinogen is not held on a polyglycolic acid bioabsorbable synthetic nonwoven fabric to allow for separate presence of thrombin and fibrinogen from each other till the use thereof, thereby rendering the use of an organic solvent (non-aqueous solvent) utterly unnecessary. To use an aqueous solvent in Greenawalt would fly in the face of Greenawalt, the very antithesis of obviousness, and would further destroy Greenawalt for its intended purpose. As such, the nonwoven fabric as used in the present invention is indeed well distinct and nonobvious from the paper-like product disclosed in Greenawalt not only from their process for preparation but also their physical structure.

Applicants' comments on the effects to be exerted by the present invention are as follows: The present invention is based on finding that, among a variety of bioabsorbable materials, a bioabsorbable nonwoven fabric made of polyglycolic acid may advantageously be used for a topical hemostatic material due to its appropriate elasticity and flexibility to ensure valid sealing as well as excellent operability and easy handling when used for topical hemostatic to ultimately exert excellent hemostatic efficacy. Greenawalt discloses a hemostatic material wherein a bioabsorbable polymer such as polyglycolic acid holds thrombin and fibrinogen, but Greenawalt does not disclose or make obvious the claimed subject matter including utilizing a nonwoven fabric made of polyglycolic acid.

Besides, the process disclosed in Greenawalt involves dissolving the components of the hemostatic composition in an organic solvent, i.e. a non-aqueous solvent such as ethanol. In contrast, the claimed process (claim 14) does not involve the use of an organic solvent but instead utilizes "a saline or buffer solution containing thrombin" as amended.

Furthermore, in comparison with a fibrin adhesive in sheet where components of a fibrin adhesive, i.e. both thrombin and fibrinogen, are fixed on a collagen sheet (TachoComb), a polyglycolic acid bioabsorbable synthetic

nonwoven fabric according to the present invention exhibits much better, excellent hemostatic efficacy as demonstrated in Examples of the present specification.

There are variety of differences between the present invention and the prior art as pointed out above. Even if the combinations as proposed were obvious (not necessarily conceded by applicants), the result and reconstruction of Greenawalt in view of the secondary references would still not reached the claimed subject matter for the reasons pointed out above. Withdrawal of the rejection is in order and is respectfully requested.

Applicants respectfully submit that all the issues raised in the final action are addressed above in such a way as to result in allowance of applicants' claims. Accordingly, applicants respectfully request favorably reconsideration, entry of the amendments presented above, and early formal allowance.

Respectfully submitted,

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